REMARKS

Claims 5, 8, 9, and 11-29 are pending in the application. Claim 5 has been allowed. Claims 8, 9 and 11-21 have been withdrawn from consideration as being directed to a nonelected invention and are hereby cancelled without prejudice to the Applicants' right to refile those claims in a related application.

The error at page 25, line 2 of the specification of the application as originally filed is corrected by the instant amendment of the specification.

The instant amendments to claims 22 and 27 obviate the outstanding rejections of claims 22-25 and 27-29 under 35 U.S.C. § 112, ¶ 1: the term "equivalent", which was objected to by the Examiner, has been deleted.

Applicants bring the following information to the attention of the Examiner. A review by Applicants undertaken in connection with the preparation of this response confirmed that, on best present information, R&D Systems, Inc. (Minneapolis, MN) offered a recombinant human TGF-β sRII:F_c chimera for sale in the United States beginning in July 1997. This date of first sale has been confirmed by R&D Systems; Applicants presently have no basis to confirm this date of first sale independently. As the July 1997 date of first sale provided by R&D Systems is after the April 18, 1997 effective filing date of the instant application, Applicants presently understand that the R&D Systems's July 1997 offer for sale does not constitute prior art to the pending claims.

The Examiner has maintained her rejections of claims 22-26 and claims 28 under 35 U.S.C. § 103(a) ("Section 103(a)") as being unpatentable as obvious in light of U.S. Patent No. 6,046,157 ("*Lin*") in view of U.S. Patent No. 5,605,690 ("*Jacobs*"). Per the Examiner, it would have been obvious to combine *Lin's* disclosure that amino acids 1-166 of SEQ ID NO: 8 (*Lin*, column 9, lines 13-19) can be used as a soluble receptor that binds to TGF-β and *Jacobs's* disclosure of fusion proteins with a soluble TNF receptor and IgG1 (*Jacobs*, column 7, lines 41-58) to arrive at the claimed invention. According to the Examiner, "[t]o take a known protein with known properties and fuse it to another known protein with known properties is not an unpredictable process." April 17, 2004 Office Action, p. 4. In the Examiner's view, the fact "[t]hat *Lin*

did not disclose a fusion protein ...does not indicate it was not obvious to make such a protein." *Id.*

As explained hereinafter, the Examiner's obviousness rejections are grounded in impermissible hindsight and lack legal and factual support.

"Combining prior art references without evidence of such a suggestion, teaching or motivation simply takes the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability – the essence of hindsight." *In re Dembiczak*, 175 F.3d 994 (Fed. Cir. 1999).

Even if *Lin* and *Jacobs* could be combined and modified as suggested by the Examiner, such fact would not have made the combination and modification of those two prior art references obvious unless the prior art suggested the desirability of the modification. *In re Gordon*, 733 F.2d 900 (Fed. Cir. 1984). *See also In re Kotzab*, 217 F.3d 1365 (Fed. Cir. 2000)(the ease with which a combination of prior art may be understood today does not equate to a motivation in the art, at the time the claimed invention was made, to combine the prior art to render the claimed invention obvious).

Beyond failing to cite the requisite motivation to combine *Lin* and *Jacobs* as suggested, the Examiner also ignores critical differences between *Lin's* TGF-β receptor protein and *Jacob's* TNF receptor protein which would have discouraged skilled artisans from making the combination advocated by the Examiner.

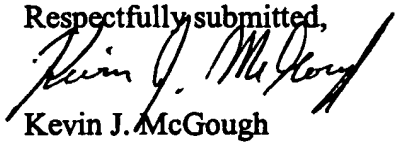
The attached declaration of Dr. Richard Cate attests to the difficulties encountered in the prior art with expression of analogous fusion proteins and provides further support for the Applicants' contention that the invention of the pending claims was nonobvious. Dr. Cate's description of the difficulties he encountered in attempting to express an AMH-RII fusion protein refute the Examiner's contention that – as of the date of the invention - "[t]o take a known protein with known properties and fuse it to another known protein with known properties is not an unpredictable process." April 20, 2004 Office Action; page 4.

Prior to the date of the instant invention, AMH-RII was a known protein and the constant region of the immunoglobulin to which Dr. Cate sought to fuse AMH-RII was

known. Yet Dr. Cate attests to the fact that he was unable to express the AMH-RII fusion protein. According to Dr. Cate, an attempt to express a fusion protein as of the date of the instant invention was not guaranteed to succeed.

In light of all of all of the foregoing, Applicants respectfully submit that each of the pending claims are patentable and are in a condition for allowance. Accordingly, Applicants respectfully request that each of the pending claims be passed to issue.

Respectfully submitted,



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